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the variable heavy and light domains of an antibody selected from the group consisting of 16C10, 7C10, 20C9 and 7B6, and wherein said amino acid sequences correspond to those set forth in SEQ. ID NOS. 1-12.

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14. (Amended) The transfectoma of Claim 13, wherein said cell expresses a primatized antibody having the amino acid sequence set forth in any one of Figures 8a, 8b, 9a, 9b, 10a and 10b, as set forth in SEQ. ID NOS. 1-12.

REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, and in light of the remarks which follow, are respectfully requested.

By the present amendments, Claims 1-4 and 15-20 have been cancelled in order to expedite prosecution. Also, new Claims 21-26, which are directed to compositions containing primatized antibodies according to the subject invention, have been presented. Further, Claims 5 through 12 and 14 have been amended in order to obviate outstanding §112 issues.

Turning now to the Office Action, the objection to the Figures is noted. Applicants respectfully advise that formal figures will be submitted upon allowance.

The objection to the specification is also noted. The specification has been reviewed for errors.

Claims 15-20 stand rejected under 35 U.S.C. §112, first paragraph, as being non-enabled. This rejection should be moot as these claims have been cancelled in order to expedite prosecution. However, Applicants respectfully maintain that the subject application adequately establishes that the subject primatized antibodies which specifically bind human B7.1 are useful therapeutic agents, in particular because of their binding specificity, as well as their being of primate origin. Specifically, because they comprise primate variable domains and human constant domains, they should elicit little or no immunogenic response and should effectively inhibit B7 antigen mediated T-cell responses. Therefore, they should be useful in treating diseases involving human B7.1/CD28 interactions.

The rejection of the claims on the basis that Applicants have not adequately enabled antibodies that specifically bind B7.1 and/or B7.2 is also moot based on the present amendments, i.e., cancellation of Claims 1-4 and amendment of Claim 12, to recite that the primatized antibody binds to human B7.1.

The claims also are rejected because they assertedly require specific vector systems (disclosed in cited, commonly-assigned patent applications), as well as primatization protocols (also disclosed in a commonly-assigned patent application). Therefore, the Office Action indicates that the incorporation by

reference of the subject matter to these applications may be improper, in particular if the incorporated subject matter is essential to the invention.

Applicants submit that such incorporation is not improper. Specifically, while these vector systems and primatization protocols are preferred, they are not essential to the invention. To the contrary, the subject application provides the complete DNA and amino acid sequences of the subject primatized antibodies. Thus, these antibodies could be synthesized without the need to rely upon the incorporated protocols and vector systems.

Moreover, Applicants respectfully advise that the incorporation by reference to such applications would be permissible, even assuming the subject matter were essential, as the cited applications now stand allowed. As noted in the Office Action, it is proper to incorporate essential material by reference to allowed U.S. applications. Therefore, withdrawal of the §112, first paragraph, rejections are respectfully requested.

Claims 2-11 and 14-20 stand rejected under 35 U.S.C. §112, first paragraph, as assertedly requiring the availability of unique biological materials that therefore should have been publicly deposited. This rejection is respectfully traversed to the extent it may be applicable to the claims as amended.

In particular, Applicants note that all of Claims 5-14 and 21 require that the antibody contain the variable heavy or light

domains of specific antibodies, the complete sequences of which are provided in the subject application. In this regard, the Examiner is respectfully referred to the figures and the previously submitted sequence listings. Therefore, no deposit should be necessary as the specification provides enough information to allow one skilled in the art to synthesize these antibodies absent undue experimentation. Accordingly, withdrawal of the §112, first paragraph, rejection of Claims 2-11 and 14-20 is respectfully requested.

Claims 1-20 further stand rejected under 35 U.S.C. §112, first paragraph, as being indefinite. This rejection is respectfully traversed to the extent it may be applicable to the claims as amended.

The objection to "B7.1 and/or B7.2 antigen" should be moot based on the cancellation of Claims 1-4 and the amendment of Claim 12. Applicants note that the claims now recite that the antibody binds to human B7.1, which comprises adequate support in the disclosure. Moreover, the criticism with respect to "depleting" and "non-depleting" should also be moot given the cancellation of the claims which contained these phrases.

The criticism of "16C10, 7C10, 20C9 and 7B6" is respectfully traversed. Applicants respectfully submit that the meaning of these terms would be apparent to one skilled in the art when the claims are construed in view of the specification. There-

fore, there is no §112 indefiniteness problem with respect to this nomenclature.

The criticisms of Claims 6-11 and 14-20 are believed to be moot as the claims now refer to the sequence ID numbers corresponding to the recited sequences.

The criticism of "human B7.1" as being an arbitrary protein designation is respectfully traversed. As evidenced by the extensive number of literature references which are referenced in the subject application (that refer to this antigen by the same name as Applicants and which were available at the time of the invention), it is readily apparent that human B7.1 is an accepted, art-recognized name for a unique human antigen. Therefore, contrary to the Office Action, Applicants respectfully submit that the claims do distinctly point out and claim what is intended. Indeed, this is readily apparent from the references cited at pages 9-11 of the subject application which refer to this protein as B7.1.

Finally, the criticism with respect to the claims that refer to therapeutic treatment is moot as Claims 15-20 have been cancelled. Therefore, withdrawal of the previous §112, second paragraph, rejection of Claims 1-20 is respectfully requested.

Claims 1-20 further stand rejected under 35 U.S.C. §103 as being unpatentable over the combination of Linsley et al (*Ann. Rev. Immunol.*, 1993) or Linsley et al (USP 5,434,131), or Linsley et al (USP 5,521,288), taken in view of Cohen (*Science*,

1993), Hathcock et al (*Science* 1933), Freeman et al (*Science*, 1993), Freeman et al (*Science*, 1993), and "art-known procedures and motivation to produce primatized antibodies for diagnostic and therapeutic regimens" as assertedly acknowledged at pages 14-26 and 21-27 of the specification (Newman et al, *Biotechnology*, 1992). This rejection is respectfully traversed to the extent it may be applicable to the claims as amended.

At the outset, Applicants respectfully advise that all of the subject claims are now limited to primatized antibodies which contain specific sequences which are contained in SEQ. ID NOS. 1-12. Applicants further respectfully submit that the combination of references would not teach or suggest antibodies containing these specific sequences.

To the contrary, the Linsley et al references merely teach the role of CD28:B7 interactions in regulating responses and generically suggest producing antibodies having such binding specificity. However, none of these references teach or suggest the particular primatized antibodies claimed herein. Indeed, the references do not even suggest producing primatized antibodies.

Cohen, Hathcock et al, and Freeman et al admittedly teach the structure and function and the apparent contribution of B7.1 and B7.2 in regulating immune responses either and the potential use of ligands having specificity thereto in therapeutic regimens. However, as with the primary references, none of these

references teach or suggest production of a primatized antibody which specifically binds human B7.1 antigen.

Also, it is acknowledged that at the time of the invention methods for producing primatized antibodies had been disclosed. In particular, the present assignee had published references and had published patents applications relating to production of primatized antibodies. However, Applicants respectfully submit that, notwithstanding such disclosure, it would not have been obvious that such techniques would necessarily be applicable to human B7.1. In particular, it would not have been known that primates would be able to generate an effective immune response against human B7.1 antigen, given the substantial likelihood that this antigen would be conserved in humans and in other primates. It would have been reasonably expected that such antigen would be conserved in different primates given its important role in regulating the immune system. Therefore, it would not have been reasonably expected that primates would recognize human B7.1 antigen as foreign and therefore elicit antibodies thereto.

Moreover, even assuming *arguendo* that it would have been reasonably predicted that antibodies could be produced in primates, it could not have been reasonably expected that primate antibodies having the specific amino acid sequence of 7B6, 16C10, 7C10, and 20C9 would have been obtained. Nor could it have been reasonably predicted that primatized antibodies pos-

sessing the specific properties of these antibodies, i.e., binding affinity, ability to inhibit IL-2 production, would have been obtained.

This could not have been reasonably predicted given the well established unpredictability associated with monoclonal antibodies even those produced against a specific antigen. Given this inherent unpredictability and variability, it would not have been obvious, based on the references cited by the Examiner, that an antibody possessing the specific characteristics of any of 16C10, 7C10, 20C9 and 7B6 would have been obtained.

Therefore, Applicants respectfully request withdrawal of the outstanding §103 rejection based on Linsley et al (three cited references), taken in view of Cohen, Hathcock et al, Freeman et al, and art known procedures.

Based on the foregoing, the subject application is believed to be in condition for allowance. A Notice to that effect is respectfully solicited. However, if any issues remain outstanding after consideration of this Reply, the Examiner is

respectfully requested to contact the undersigned so that prosecution can of this application may be expedited.

Respectfully submitted,

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